Efficient capture of high-quality data on outcomes of treatment for macular diseases: The Fight Retinal Blindness! Project

Gillies, M C ; Walton, R ; Liong, J ; Arnold, J J ; McAllister, I ; Morlet, N ; Hunyor, A ; Guymer, R ; Keeffe, J ; Essex, R ; Herrera-Bond, A ; Glastonbury, B ; Simpson, J M ; Barthelmes, D

Abstract: PURPOSE: To describe the development of a web-based high-quality data collection tool to track the outcomes of treatment of macular disease in routine practice. METHODS: Testing of a larger data collection tool established which fields a clinician would reliably fill out. The program, which was developed using freely available software, consists of modules interacting with a core system. The module for neovascular age-related macular degeneration is described here. RESULTS: Data for initial visits can be entered within 30 seconds, 15 seconds for follow-up visits. Fifteen centers from Australia, New Zealand, and Switzerland are currently contributing data. Finalized data from 2,052 eyes of 1,693 participants dating from January 2006 were analyzed. Median (25th and 75th percentiles) visual acuity at the index visit was 55 (41, 68) logarithm of the minimum angle of resolution letters with the following lesion types: minimally classic 17.2%, predominantly classic 24.6%, occult 52.0%, idiopathic polypoidal choroidal vasculopathy 1.2%, and retinal angiomatous proliferation 3.2%. CONCLUSION: This software tool will facilitate the collection of large amounts of data on the routine use of treatments of neovascular age-related macular degeneration. This will allow us to analyze important potentially modifiable variables, such as the effect of different treatment patterns on visual outcomes, and to evaluate new treatments as they are introduced into practice.

DOI: https://doi.org/10.1097/IAE.0b013e318296b271

EFFICIENT CAPTURE OF HIGH-QUALITY DATA ON OUTCOMES OF TREATMENT FOR MACULAR DISEASES

The Fight Retinal Blindness! Project

MARK C. GILLIES, MBBS, PHD, FRANZCO,* RICHARD WALTON, MSC,* JULINES LIONG, BSC,† JENNIFER J. ARNOLD, MBBS, FRANZCO,‡ IAN MCALLISTER, MBBS, FRANZCO,§ NIGEL MORLET, MBBS, FRANZCO,¶ ALEX HUNYOR, MBBS, FRANZCO,** ROBYN GUYMER, MBBS, PHD, FRANZCO,†† JILL KEEFFE, PHD,†† ROHAN ESSEX, MBBS, FRANZCO,‡‡ AMPARO HERRERA-BOND, DIP.APP.SC.(ORTHOP), B.BUS.,* BRIONY GLASTONBURY, MHSM,* JUDY M. SIMPSON, PHD,§§ DANIEL BARTHELMES, MD, PHD, FEBO*¶¶

Purpose: To describe the development of a web-based high-quality data collection tool to track the outcomes of treatment of macular disease in routine practice.

Methods: Testing of a larger data collection tool established which fields a clinician would reliably fill out. The program, which was developed using freely available software, consists of modules interacting with a core system. The module for neovascular age-related macular degeneration is described here.

Results: Data for initial visits can be entered within 30 seconds, 15 seconds for follow-up visits. Fifteen centers from Australia, New Zealand, and Switzerland are currently contributing data. Finalized data from 2,052 eyes of 1,693 participants dating from January 2006 were analyzed. Median (25th and 75th percentiles) visual acuity at the index visit was 55 (41, 68) logarithm of the minimum angle of resolution letters with the following lesion types: minimally classic 17.2%, predominantly classic 24.6%, occult 52.0%, idiopathic polypoidal choroidal vasculopathy 1.2%, and retinal angiomatous proliferation 3.2%.

Conclusion: This software tool will facilitate the collection of large amounts of data on the routine use of treatments of neovascular age-related macular degeneration. This will allow us to analyze important potentially modifiable variables, such as the effect of different treatment patterns on visual outcomes, and to evaluate new treatments as they are introduced into practice.

RETINA 0:1–8, 2013

Unprecedented advances in the treatment of macular diseases over the last decade have prevented vision loss and blindness in many people. The discovery that vascular endothelial growth factor is a major driver of angiogenesis and vascular leak in the eye provided the rationale for Phase 3 clinical trials that demonstrated the efficacy of the vascular endothelial growth factor inhibitors. These studies examined ranibizumab (MARINA, ANCHOR),[1,2] bevacizumab (CATT),[3,4] and aflibercept (VIEW 1 and 2)[5] for neovascular age-related macular degeneration (AMD). Diabetic macular edema and retinal vein occlusion are additional indications for vascular endothelial growth factor inhibitors.[6–9] Intravitreal steroid therapy may also have a role in the treatment of macular edema,[10] particularly as agents formulated for the eye become available (FAME study[11]).

Clinical trials determine whether new treatments work in highly controlled conditions for a highly selected group of patients that may not be representative of the general patient population with the disease. The high experimental, or internal, validity of a clinical trial comes at a cost of generalizability, or external validity, of its results. An important question, therefore, is whether the promising results of pivotal clinical trials translate to successful patient outcomes in the general patient population under real-life conditions. These questions are best answered by population-based postmarketing observational studies.

Postmarketing surveillance refers to the ongoing evaluation of a drug after its regulatory approval.

Growing concerns about the safety of new medicines, and increasing awareness of the potential benefits of using large-scale population-based data to monitor product safety and effectiveness, have placed new emphasis on the late-phase research agenda. Evidence from such research has led to subsequent withdrawal of drugs that had initially seemed promising in Phase 3 studies, such as cerivistatin (Lipobay, Bayer A.G.)[12] or rosiglitazone (Avandia, GlaxoSmithKline).[13] By monitoring the general patient population undergoing varied and individualized treatment regimens, postmarketing observational studies complement earlier clinical trials. They may determine small but significant treatment effects in routine clinical practice by tracking patients for longer and collecting a different broader set of end points, including safety, patient preference, quality of life, and long-term effectiveness.

The Fight Retinal Blindness! (FRB!) Project has designed an efficient web-based data collection tool specifically to track the outcomes of treatment of macular disease in routine clinical practice. It is anticipated that this "registry" will allow us to confirm whether outcomes of treatment in routine practice of the new drugs for macular disease are consistent with the promising results observed in the pivotal clinical trials. We will compare different dosing regimens for their ocular safety, long-term effectiveness, and patient acceptance. We will also compare the outcomes achieved by each individual drug in various clinical settings. The system will allow individual physicians to review their own data and compare their own results against national benchmarks. In this study, we describe the principles of design and development of this tool.

From the *Save Sight Institute, Sydney Medical School, University of Sydney, Sydney, Australia; †Information and Communications Technology, University of Sydney, Sydney, Australia; ‡Marsden Eye Specialists, Parramatta, New South Wales, Australia; §Lions Eye Institute, Center for Ophthalmology and Vision Science and ¶Department of Population Health, University of Western Australia, Perth, Australia; **Retina Associates, Chatswood, Sydney, Australia; ††Department of Ophthalmology, Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Melbourne, Australia; ‡‡Department of Ophthalmology, Canberra Hospital, Canberra, Australia; §§Sydney School of Public Health, University of Sydney, Sydney, Australia; and ¶¶Department of Ophthalmology, University Hospital Zurich, Zurich, Switzerland.

Supported by a grant from the Eye Foundation (2007–2009) and a grant from the National Health and Medical Research Council, Australia (NHRMC 2010-1012).

M. C. Gillies is a Sydney Medical Foundation Fellow, M. C. Gillies and R. Guymer are supported by the National Health and Medical Research Council practitioner fellowships. D. Barthelmes was supported by the Walter and Gertrud Siegenthaler Foundation Zurich, Switzerland, and the Swiss National Foundation.

Reprint requests: Mark C. Gillies, Save Sight Institute, South Block, 8 Macquarie Street, Sydney NSW 2000, Australia; e-mail: mark.gillies@sydney.edu.au

Methods

Structure of the Fight Retinal Blindness! Project

The FRB! Project consists of a Steering Committee, an Executive Committee, a Publishing Committee, and User groups. The Steering Committee, which is elected at an annual meeting of Users in each country, oversees the general development of the project, data analysis, and publication, and coordination of the different interests and requests from the User groups. The Publishing Committee monitors publications and adherence to the participation and publishing guidelines. The User groups are responsible for the development of new modules or the modification of existing modules. For the purposes of this study, "Users" are those entering data with the software, whereas "Participants" are those whose outcomes are tracked.

Software and System Design

Because the high prevalence of neovascular AMD has rendered many retinal practices very busy, it was believed critically important to reduce the load of data capture by clinicians. Therefore, the choice of data fields was guided by parsimony, validity, and focus on achieving the registry's purpose to track and evaluate current and emerging treatments of macular disease in routine practice after they have been approved.[14] Trialing a system with a large range of data fields in one nonacademic and three academic retinal practices revealed the minimum data fields that practitioners would consistently complete. Demographic data along with logarithm of the minimum angle of resolution (logMAR) visual acuity and intraocular pressure may be entered by clinical assistants. All other fields must be entered by the treating physician.

Quality assurance (QA) measures were included to ensure that only verified and high-quality data are entered into the system. Data can be "Saved" if not all the mandatory data are available or entered. When all mandatory fields have been filled, the User can "Finalize" the visit, starting a built-in validation process that checks whether all mandatory fields have been completed and that values are within predetermined ranges, for example, visual acuity must be between 0 and 100 letters. Only when data are finalized, they are available for subsequent analysis and reporting. The system has been designed in such a way that it will not allow a visit to be finalized unless all the fields have been filled and all numerical data fall within prespecified ranges.

The software used in the FRB! Project consists of modules interacting with a core system. The core system provides a range of basic functions, which are used by each module for patient data management. Each module provides the user with the functionality to capture data for a specific purpose, in the first instance to collect data from patients receiving treatment of neovascular AMD. The core system is modified and changed only under very specific circumstances, which have been approved by the Steering Committee. Each user and user group, however, may create or change modules which they can share with other users should they be interested. Each registered FRB! Project user can use the full scope of the software or select only modules that fit their needs.

The FRB! software is a web-based application, which was developed using freely available software such as Apache, MySQL, PHP, and RubyonRails. This approach allows the application to be run on different server operating systems. Any device with Internet access and a recent browser can be used to interact with the application.

There are two ways of entering data into the FRB! system: via a web interface or via a third-party software interface. If the User has no electronic patient management system, the independent web-based application, which can be accessed from a wide range of devices and operating systems (e.g., Windows-PC, Macintosh, tablet computer, mobile phone), can be used with a regular browser (e.g., Safari, Internet Explorer, Firefox, Opera). Additional software on the user's terminal is not required. If the user has an electronic patient management system, this can be modified so that data can be automatically transmitted electronically to the project database, thus simplifying and expediting the process for the user through single-point data entry.

Participant-reported outcomes are collected using instruments such as the Impact of Vision Impairment questionnaire.[15] Responses are collected using a specially adapted application for tablet computers catering for the special needs of the visually impaired, enabling participants to choose color schemes and font sizes. Data acquired using a tablet are transmitted directly to the FRB! database for further analysis. The collection of PROs will facilitate studies to determine whether improvements in visual acuity measured on a chart are associated with improvement in visual function and participant well-being.

Data Anonymity and Security

The FRB! Project software is designed to provide maximum data security and anonymity. Users can enter patient data into the respective module of the FRB! software in an anonymized way. The system then generates a unique identifier (string of numbers and letters) specific to each participant. This allows for complete tracking of outcomes, even if the participant is treated for different conditions by different doctors at different locations. As well as the unique identifier, demographic data, such as the date of birth, gender, initials, and ethnicity, are also stored. No other personal information is recorded. All data transmissions between the user and the server are encrypted using 128-bit encryption (Secure Sockets Layer). The data are stored and backed up on secure servers at The University of Sydney's Information and Communication Technology Department.

Anonymity of users is also closely guarded. Individual Users can only see their own data and summary descriptive data from their own country with which they may compare their own outcomes. Users can withdraw their data from the database at any time, without providing a reason.

Ethical Considerations

Activities conducted by a health care provider, which aim to monitor, evaluate or improve the quality of care provided, are QA studies. The Australian Health Ethics Committee considers that QA activities are an essential and integral part of health care delivery that should be encouraged and facilitated.[16] Quality assurance includes quality improvement activities such as medical, clinical, and record audit and observational studies, to which the ethical principles of research apply. Clinical registries are established and operated with the aim of improving patient care and outcomes through greater understanding of events, treatments, and outcomes,[17] thus meeting the definition of a QA activity.

A unique computer-generated string is assigned to a patient automatically when their details are first entered into the system. This string makes the patient unique in the database; it is not visible to the User. It is linked to the User(s) own practice identifiers for each patient. When the User subsequently enters the follow-up data, the practice identifier for that User can be selected to create a follow-up visit. As an additional measure to ensure that the right data are being entered for the right patient, initials and date of birth are shown.

Data registries must satisfy relevant regulations and the requirements of the appropriate institutional Human Research Ethics Committee (HREC), which may vary from place to place. "Opt in" informed patient consent, which greatly increases the onus of work on the treatment provider and which can result

in recruitment rates as low as one in six,[18] may not be necessary if all patients attending a practice consent to the use of their anonymized data for clinical audit and research purposes. Since the information collected in the FRB! system is usually routinely collected by the treating doctor and since the activity meets the requirements for a QA activity and does not breach individual patient confidentiality, HREC approval was sought in Australia to conduct the Project as a QA or quality improvement activity.

Each participating core center obtained approval from their respective HREC to conduct the Project as a QA activity. Overarching ethical approval was also obtained from the Royal Australian and New Zealand College of Ophthalmologists' HREC to streamline the process for participating private practices and to ensure, from a central governance perspective, that all users were aware and informed of their ethical responsibilities. Documentation of HREC approval from each center is copied to the central governing office to ensure currency of approval is maintained.

Data Export

Since the FRB! Project software is designed to be a research tool, data export and analysis features are very important. Individual Users can download their own data at any time as a text file in comma separated variable format. The software also offers statistical tools for simple analyses. Users can export their own data and analyze it as they see fit for more sophisticated analyses.

Statistical Methods

We calculated descriptive statistics for participants at the Index visit, defined as the first visit at which an intervention was commenced. For any cases where a single patient contributed two eyes, only one was randomly chosen for analysis to remove the possibility of within-patient correlation biasing the results. For continuous variables, we calculated the mean or median and 25th and 75th percentiles. We summarized categorical variables as percentages; participants with missing data were not included in the denominator. All analyses were performed with R version 2.15.0.[19]

Results

Data Fields for the Neovascular Age-Related Macular Degeneration Module

The data captured by the FRB! application were kept to a minimum to deliver an efficient data collecting tool. As a result of our experience with the first version, which had a large number of fields for characteristics such as disease activity, a refined set of data elements were chosen such that an Index visit could be entered in <30 seconds and a follow-up visit in <15 seconds. Version 5 of the neovascular AMD module has been operational since May 2010. The data fields for the Index visit for this module are shown in Table 1. Table 2 shows the fields for a follow-up visit.

Table 1. Data Fields for a Baseline Visit

Field	Subfield
Date of visit	
Treatment audit	
Visual acuity in logMAR	
Intraocular pressure (not mandatory)	
Ocular conditions	Early AMD
	Dry AMD
	Neovascular AMD
	Axial myopia
	Vitreomacular traction/PMF
	Posterior uveitis
	Diabetic retinopathy
	Glaucoma
	Clinically significant cataract
	Pseudophakia
	Amblyopia
Pre-treatments	Laser
	PDT
	TTT
	Triamcinolone
	Anti-VEGF Lucentis
	Anti-VEGF Avastin
	Anti-VEGF Eylea
	Other
Angiography lesion criteria	Occult
	Minimally classic
	Predominantly classic
	RAP
	IPCV
	Disciform scar
	Juxtapapillary
Greatest linear dimension	
CNV activity	Active
	Inactive
	Unsure
Treatment type	No treatment
	Anti-VEGF Lucentis
	Anti-VEGF Avastin
	Anti-VEGF Eylea
	Triamcinolone
	TTT
	Laser
	PDT

CNV, choroidal neovascularization; PDT, photodynamic therapy; VEGF, vascular endothelial growth factor; PMF, premacular fibrosis; TTT, transpupillary thermotherapy; IPCV, idiopathic choroidal vasculopathy; RAP, retinal angiomatous proliferation.

Table 2. Data Fields for Follow-up Visits

Field	Subfield
Date of visit	
Treatment audit	
Visual acuity in logMAR	
Intraocular pressure (not manadory)	
CNV activity	Active
	Inactive
	Unsure
Treatment type	No treatment
	Anti-VEGF Lucentis
	Anti-VEGF Avastin
	Anti-VEGF Eylea
	Triamcinolone
	TTT
	Laser
	PDT
Adverse events	Patient reported postinjection pain
	RPE tear
	Hemorrhage-reduced BCVA by >15 letters
	Infectious endophthalmitis
	Noninfectious endophthalmitis
	Retinal detachment
	Cataract extraction/other intraocular surgery
Discontinue treatment?	Treatment successful
	Further treatment futile
	Patient goes to another doctor
	Patient declines
	Medically contraindicated
	Deceased

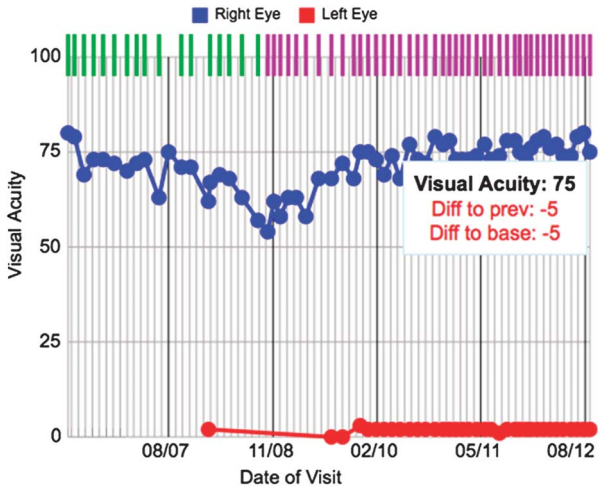
BCVA, best-corrected visual acuity; CNV, choroidal neovascularization; PDT, photodynamic therapy; RPE, retinal pigment epithelium; VEGF, vascular endothelial growth factor; TTT, transpupillary thermotherapy.

Graphical Displays

The software displays graphically visual acuity and respective treatments given over time (Figure 1). Mouse-over functionality reveals additional details such as the change in number of letters read at the selected visit compared with the previous visit and to the Index visit. An enlarged version of the graph provides further functionality such as displaying the information for each eye separately, zooming in and out, or changing the time scale. Another feature is the ability to compare the individual participant's visual response to treatment with the results of the sham-treated groups from the MARINA[1] Study and the Macular Photocoagulation Study[20] (Figure 2).

Uptake and Usage

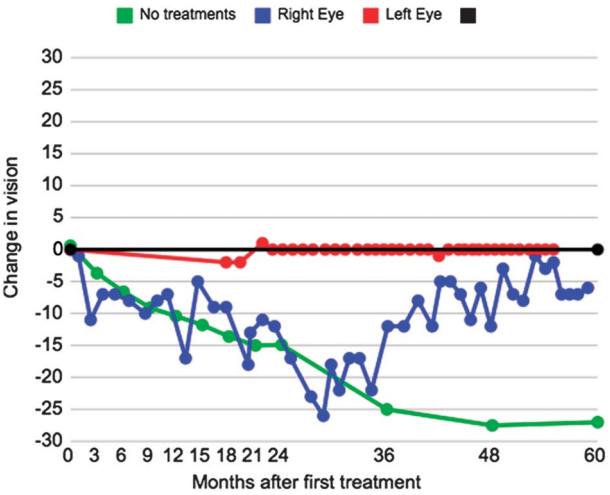
Use of the FRB! software has steadily gained momentum. Currently, 13 centers in Australia, 1 in New Zealand, and 1 in Europe are contributing data.



COLOR

Fig. 1. Visual acuity of a single patient since starting treatment in June 2006. Intravitreal treatment with bevacizumab (green bars) and ranibizumab (purple) is indicated on top of the graph. Visual acuity in the right eye declined initially then improved steadily after changing from bevacizumab to ranibizumab in October 2008 and increasing the injection frequency. Mouse-over function shows that at the last visit, visual acuity was 75 logMAR letters, the difference to the previous visits was −5 letters, and the difference to the Index visual acuity was also −5 letters.

Logarithm of the minimum angle of resolution visual acuity was measured by eight users, who tended to be from the larger academic centers, whereas five Users, more from smaller private practices, measured Snellen visual acuity which they transferred to logMAR letters using a chart that is available on the data entry screen. Royal Australian and New Zealand College of Ophthalmologists has accredited the FRB! software application as a self-audit tool that can be used to gain points under the clinical audit section of their continuing professional development program.



COLOR

Fig. 2. Visual acuity of the same patient shown in Figure 1 plotted as change in logMAR letters compared with the Index visit for each eye. The green line represents data obtained from the sham-treated groups from the MARINA and Macular Photocoagulation Study.

Participant Characteristics

Finalized data from 2,052 eyes of 1,693 participants were available for this analysis. Thirteen Users contributed data, median 104 eyes (range, 26–304). Although the proportion of eligible patients that the User tracked with the system was not audited, it was specified in the Users' agreement that data should be entered on at least 85% of patients in the User's practice that are eligible to have their data included. This is also a condition for Users applying for Continuing Professional Development points, which are a requirement for Medical Board registration in Australia.

The first recorded anti–vascular endothelial growth factor treatment was administered in January 2006. A total of 34,168 visits have been recorded with a total of 25,467 treatments. Of all participants to date, 60.9% were women; the mean (25th and 75th percentiles) age at the index visit was 79.7 (75, 85) years for women and 78.4 (74, 85) years for men. Median (25th and 75th percentiles) visual acuity at the index visit was 55 (41, 68) logMAR letters. A histogram of visual acuity at the index visit is presented in Figure 3. The lesion types were distributed as follows: minimally classic 17.2%, predominantly classic 24.6%, occult 52.0%, idiopathic polypoidal choroidal vasculopathy 1.2%, and retinal angiomatous proliferation 3.2% (others 1.8%).

Discussion

In response to the unmet need for postmarketing observational studies of the emerging treatments of macular disease, we have created an efficient web-based system to collect high-quality outcome data from routine clinical practice. The system has been designed to extract the maximum amount of information from a minimal data set to produce benefits for all stakeholders. Although postmarketing observational studies produced data that are not as clean as those from randomized clinical trials, "registries can be more evidence-based than the traditional framework of randomized controlled trials for care improvement."[21]

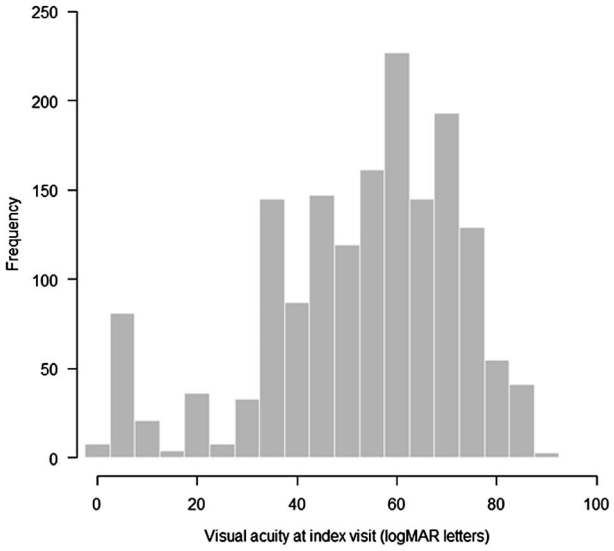


Fig. 3. Histogram of visual acuity at the index visit.

An important principle in registry design is to reduce the load of data entry.[14] Reduced burden facilitates data entry at the time of the consultation and improves data quality by limiting complexity. The collection of just the four variables, treatment, date, logMAR visual acuity, and grading of activity to active or inactive allows many important questions to be asked in people being treated for neovascular AMD. For example, different treatment patterns, such as monthly, pro re nata, and "inject and extend," can be identified and their outcomes are compared. Eyes may be matched to the Index visit of participants in pivotal Phase 3 clinical trials to establish whether their results are reproducible in the general population.

Observational registry-based studies such as this one have advantages for stakeholders at every level. Physicians get a real-world picture of current treatment patterns and outcomes. They can compare their results with those of other clinicians[22]. Physician organizations can assess the degree to which diseases are being managed according to evidence-based guidelines. Government and industry stakeholders can see how interventions are being used and what their effectiveness is in the general patient population. Pharmaceutical companies may fulfill some of their obligations for postmarketing surveillance. Data can also be used to develop new hypotheses for interventions in specific patient populations. Graphical display of an individual's visual acuity response to treatment may improve participant understanding of their disease and treatment compliance, as well as facilitating patient flow through the practice.

Some early reports of postmarketing observational studies for neovascular AMD have recently appeared. The Swedish Lucentis Quality Registry, a 12-month, open-label observational study of ranibizumab for wet AMD, reported visual acuity results after a mean of 4.7 injections over 12 months in 370 patients. The authors speculated that treatment might not have been applied sufficiently aggressively.[23] The German WAVE study of 3,633 people receiving treatment of wet AMD reported that many fewer people were accessing treatment with intravitreal therapy than expected.[24] The Swedish Macular Register (http://www.eyenetsweden.se/page/28/the-macula-register.aspx, accessed August 21, 2012) does not appear to have released any reports yet. The LUMINOUS study is an ambitious project sponsored by Novartis to track the outcomes

in 30,000 patients worldwide receiving intravitreal ranibizumab (Clinicaltrials.gov identifier NCT01318941).

Far larger observational studies that have been established in ophthalmology to monitor the outcomes of anterior segment surgery demonstrate the potential benefits of this approach. Registries commonly track safety, but they may also track long-term efficacy of interventions. The Swedish National Cataract register reported the outcomes of over 1 million cataract operations performed between 1992 and 2009.[25] They found that the risk of complications declined while outcomes improved over this period. These data serve as benchmarks against which further improvements may be measured. The European Registry of Quality Outcomes for Cataract and Refractive Surgery analyzed the outcomes of 820,000 cases performed from 2009 to 2011 to produce best practice guidelines.[26] The Australian Corneal Graft Registry, established in 1986, tracked around 15,000 penetrating corneal grafts to find that the success rate fell from 87% at 1 year to 46% 15 years after surgery.[27]

We have taken steps to minimize a number of potential biases that may affect observational studies.[14] "Information bias," in which Users may misreport the outcome of an intervention if they have a vested interest in doing so, is avoided by making User data available only to the individual User. This also reduces "selection bias," by which Users enroll only patients who have a low risk of complications. "Channelling bias" may occur when drugs with similar therapeutic indications are prescribed to groups of patients with prognostic differences, such as those who have failed first-line treatment. Our system therefore includes all possible interventions for the condition being audited and collects data on previous treatments. Loss to follow-up can be a concern if it is nonrandom. To reduce the incidence of this, we have established a referral function within the system so that participants' data can be transferred seamlessly from one service provider to another as long as they are both participating in the project.

We have described here the principles of development of a software tool that forms the basis of a registry for the outcomes of treatment of macular disease. This will allow us to analyze a number of important potentially modifiable variables, such as the effect of different treatment patterns on visual outcomes. New treatments will be evaluated as they are introduced into practice. Participation in the project, which is expected to be organized along national lines, remains open and free to individual users.

Key words: patient outcome registry, age-related macular degeneration, postmarketing observational study, vascular endothelial growth factor inhibitors.

References

1. Rosenfeld PJ, Brown DM, Heier JS, et al. Ranibizumab for neovascular age-related macular degeneration. N Engl J Med 2006;355:1419–1431.
2. Brown DM, Kaiser PK, Michels M, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med 2006;355:1432–1444.
3. Martin DF, Maguire MG, Fine SL, et al. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. Ophthalmology 2012;119:1388–1398.
4. Martin DF, Maguire MG, Ying GS, et al. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. N Engl J Med 2011;364:1897–1908.
5. Heier JS, Brown DM, Chong V, et al.; VIEW 1 and VIEW 2 Study Groups. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology 2012;119: 2537–2548.
6. Do DV, Schmidt-Erfurth U, Gonzalez VH, et al. The DA VINCI Study: phase 2 primary results of VEGF Trap-Eye in patients with diabetic macular edema. Ophthalmology 2011;118:1819–1826.
7. Mitchell P, Bandello F, Schmidt-Erfurth U, et al. The RESTORE study: ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. Ophthalmology 2011;118:615–625.
8. Abegg M, Tappeiner C, Wolf-Schnurrbusch U, et al. Treatment of branch retinal vein occlusion induced macular edema with bevacizumab. BMC Ophthalmol 2008;8:18.
9. Ehlers JP, Decroos FC, Fekrat S. Intravitreal bevacizumab for macular edema secondary to branch retinal vein occlusion. Retina 2011;31:1856–1862.
10. Gillies MC, Sutter FK, Simpson JM, et al. Intravitreal triamcinolone for refractory diabetic macular edema: two-year results of a double-masked, placebo-controlled, randomized clinical trial. Ophthalmology 2006;113:1533–1538.
11. Campochiaro PA, Brown DM, Pearson A, et al. Sustained delivery fluocinolone acetonide vitreous inserts provide benefit for at least 3 years in patients with diabetic macular edema. Ophthalmology 2012;119:2125–2132.
12. Furberg CD, Pitt B. Withdrawal of cerivastatin from the world market. Curr Control Trials Cardiovasc Med 2001;2:205–207.
13. Derosa G, Maffioli P. Peroxisome proliferator-activated receptor-gamma (PPAR-gamma) agonists on glycemic control, lipid profile and cardiovascular risk. Curr Mol Pharmacol 2012;5: 272–281.
14. Glicklich RE, Dreyer NA. Registries for Evaluating Patient Outcomes: A User's Guide. Rockville, MD: Agency for Healthcare Research and Quality; 2007.
15. Weih LM, Hassell JB, Keeffe J. Assessment of the impact of vision impairment. Invest Ophthalmol Vis Sci 2002;43:927–935.
16. NHMRC. When Does Quality Assurance in Health Care Require Independent Ethical Review? Advice to Institutions, Human Research Ethics Committees and Health Care Professionals. Sydney, Australia: NHMRC; 2003.
17. ACSQHC. Operating Principles and Technical Standards for Australian Clinical Quality Registries; 2008.
18. McNeil JJ, Evans SM, Johnson NP, Cameron PA. Clinical-quality registries: their role in quality improvement. Med J Aust 2010; 192:244–245.
19. R: A Language and Environment for Statistical Computing. 2006. Foundation for Statistical Computing, Vienna, Austria Available at: http://www.R-project.org. Accessed August 21, 2012.
20. Laser photocoagulation for juxtafoveal choroidal neovascularization. Five-year results from randomized clinical trials. Macular

Photocoagulation Study Group. Arch Ophthalmol 1994;112: 500–509.
21. Sedrakyan A. Metal-on-metal failures—in science, regulation, and policy. Lancet 2012;379:1174–1176.
22. Kennedy L, Craig AM. Global registries for measuring pharmacoeconomic and quality-of-life outcomes: focus on design and data collection, analysis and interpretation. Pharmacoeconomics 2004;22:551–568.
23. Hjelmqvist L, Lindberg C, Kanulf P, et al. One-year outcomes using ranibizumab for neovascular age-related macular degeneration: results of a prospective and retrospective observational multicentre study. J Ophthalmol 2011;2011: 405724.
24. Finger RP, Holz FG. Access to healthcare services for elderly patients with neovascular age-related macular degeneration [in German]. Ophthalmologe 2012;109:474–478.
25. Behndig A, Montan P, Stenevi U, et al. One million cataract surgeries: Swedish National Cataract Register 1992–2009. J Cataract Refract Surg 2011;37:1539–1545.
26. Lundstrom M, Barry P, Henry Y, et al. Evidence-based guidelines for cataract surgery: guidelines based on data in the European Registry of Quality Outcomes for Cataract and Refractive Surgery database. J Cataract Refract Surg 2012;3:1086–1093.
27. Williams KA, Lowe M, Bartlett C, et al. Risk factors for human corneal graft failure within the Australian corneal graft registry. Transplantation 2008;86:1720–1724.

Appendix. Full Study Group Membership for the Fight Retinal Blindness! Project

Eye Surgeons Miranda, Miranda, New South Wales, Australia (Dr. A. Hunt); Eye Associates, Sydney, New South Wales, Australia (Dr. M. Gillies and Dr. A. Hunt); Retina Associates, Chatswood, New South Wales, Australia (Dr. A. H. Hunyor, Dr. S. Fraser-Bell, and Dr. C. Younan); Marsden Eye Specialists, Parramatta, New South Wales, Australia (Dr. J. Arnold and Dr. D. Chan); Gladesville Eye Specialists, Gladesville, New South Wales, Australia (Dr. S. Young); Hornsby Eye Specialists, Hornsby, New South Wales, Australia (Dr. S. Lal); Northern Rivers Eye Surgeons, Lismore, New South Wales, Australia (Dr. G. Clark and Dr. N. Aboud); Eyemedics, Adelaide, South Australia, Australia (Dr. S. Lake, Dr. R. Phillips, and Dr. M. Perks); Canberra Hospital, Garran, ACT, Australia (Dr. R. Essex); Cairns Eye and Laser Clinic, Cairns, QLD, Australia (Dr. A. Field); Queensland Eye Institute, South Brisbane, QLD, Australia (Dr. T. Kwan); Lions Eye Institute, Nedlands, Western Australia, Australia (Prof. I. McAllister, Ass Prof. F. Chen, Dr. T. Isaacs, and Prof. I. Constable); Centre for Eye Research Australia, East Melbourne, Victoria, Australia (Prof. R. Guymer, Dr. R. Troutbeck, and Dr. D. Louis); Cheltenham Eye Centre, Cheltenham; Bayside Eye Specialists, Brighton East; Southern Eye Centre, Frankston, Victoria, Australia (Dr. D. Louis); Victoria Parade Eye Consultants, Fitzroy, Victoria, Australia (Prof. R. Guymer, Dr. L. Lim, and Dr. A. Harper); Doncaster Eye Centre, Doncaster, Victoria, Australia (Dr. S. Wickremansinghe and Dr. L. P. Chow); Caulfield Eye Clinic, Caulfield, Victoria, Australia (Dr. R. Troutbeck and Dr. S. Wickremasinghe); Specialists Eye Group, Glen Waverly, Victoria, Australia (Dr. S. Wickremasinghe and Dr. L. P. Chow); Eye Institute, Auckland, New Zealand (Dr. P. Hadden); ADHB, Auckland, New Zealand (Dr. D. Squirrell); Milford Eye Clinic, Auckland, New Zealand (Dr. D. Squirrell); University Hospital Zurich, University of Zurich, Zurich, Switzerland (Dr. D. Barthelmes); Retina Specialist Auckland, New Zealand (Dr. D. Sharp, Dr. R. Barnes, and Dr. P. Hadden).